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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,521	09/01/2006	Hiroharu Kawahara	125192.00501	1684

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EXAMINER	
KIM, ALEXANDER D	
ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,521	KAWAHARA, HIROHARU	
	Examiner	Art Unit	
	ALEXANDER D. KIM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-18 and 20-33* is/are pending in the application.

4a) Of the above claim(s) *8-18* is/are withdrawn from consideration.

5)☒ Claim(s) *20,21 and 31* is/are allowed.

6)☒ Claim(s) *22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *transfection, clone*.

DETAILED ACTION

Application Status

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/03/2009 has been entered.

Applicants' amendment canceling Claims 1-7 and 19 and adding new Claims 22-31 in the paper of 03/30/2009 is acknowledged. Claims 8-18 and 20-33 are pending in the instant office action. Claims 8-18 are withdrawn as being drawn to non-elected invention.

Claims 20-31 will be examined herein.

Withdrawn-Objections to the Specification

2. The previous specification objection for disclosing "KMS. 12BM", whereas it should be ---KMS-12BM---, is withdrawn by virtue of Applicants' amendment (as noted in the previous advisory action, mailed on 12/24/2008).

Withdrawn-Claim Objections

3. The previous objection of Claims 20 and 21 for reciting "SC-02MFP" or "SC-01MFP" is withdrawn by virtue of applicants' amendment (i.e., consistent in claims and instant specification).

Claim Objections

4. Claims 27-28 are objected to because of the following informalities:

(a) Claim 27 is objected to in the recitation of "transfecting a gene…into the human cell strain" and in order to improve claim form, it is suggested that the noted phrase be amended to recite, *e.g.,* "transfecting the human cell strain with a gene encoding a desired protein".

(b) Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 28 recites the method step "further comprising culturing the transfected human cell", which does not further limit the human cell of claim 27.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 22-28 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 (Claims 23-28 dependent therefrom) recites "90% rate of cloning". However, it is unclear how a skilled artisan is to calculate the rate of cloning because the meaning of the term, particularly with respect to the term “cloning” is unclear in the context of the noted phrase. The instant specification does not define the term "cloning" and the art recognized meaning of “cloning” is "make multiple identical copies of (a DNA sequence)" by transforming or transfecting a host cell with a vector, for example; "to create or propagate (an organism) from a clone cell"; or "to produce a copy of" as shown by the American Heritage Dictionary (see attachment for the definition of "cloning"). Because the instant claim is drawn to the human myeloma cell, for purposes of examination, the term “cloning” is interpreted as being able to propagate by cell division, for example. Appropriate clarification is required.

Claim 22 also recites two “selecting clones” steps, *i.e.,* steps b) and d), and goes on to recite “wherein the clones selected”. It is unclear as to which “selected” clones the wherein clause refers – clones selected in step b), clones selected in step d), or clones selected in steps b) *and* d). It is suggested that applicant clarify the meaning of the noted phrase. In the interest of advancing prosecution and giving claims their broadest reasonable interpretation, the "clones selected" have been interpreted as being any of clones selected in step b), clones selected in step d), or clones selected in steps b) *and* d).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 22-25 and 27-30 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 22 and 29 are drawn to a human cell strain obtained from mutation of any human myeloma cell strain wherein the human cell may be capable of continuous production of a protein from any exogenous gene at a yield of 1 ng-10 ug/day per 1,000,000 cells for at least a 2-month period or at least over a 2 month period. Claims 23-25 and 27-28 are drawn to the human cell strain prepared by further comprising steps recited in claims therein. Claim 25 or 30 is drawn to the human cell of Claim 22 or 29, respectively; wherein the human cells are mutated RPMI8226 or KMS-12BM cells; wherein the mutation includes any change or alternatively just labeled as mutated in view of the fact that it is selected after the mutation induction regardless of whether or not any mutation has occurred or not.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical

name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these (paraphrased from *Enzo Biochemical Inc. v. Gen-Probe Inc.* (CAFC (2002) 63 USPQ2d 1609).

The instant specification teaches two representative species of the genus of human cell strains, *i.e.,* human cell strains SC-02MFP (Accession Number FERM BP-10078) or SC-01MFP (Accession Number FERM BP-10077). However, the genus of claimed human cell strains includes any human cell strain (including but not limited to any mutant strain of any human myeloma cell) which may be capable of producing a protein from any exogenous gene at a yield of 1 ng-10 ug/day per 1,000,000 cells for at least a 2-month period or at least over a 2 month period; because the protein production capability recited in the claims can be interpreted as a requirement for the cell *before* the mutation wherein the claimed human cell is the mutated version, which is also supported by the summary of the invention. Furthermore, Claims 22 and 29 (Claims 23-25, 28 and 30 dependent therefrom) encompasses any human cell strain having a

product by process type limitation, which “ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS” (see MPEP 2113 [R-1]). In the instant case, the only structure implied by the steps is that the claimed human cell strain has to be originated from a human myeloma cell; whereas the obtaining and selecting step (although it describes the physical characteristics) does not contribute or imply any structure of the claimed human cell strain. It is noted that Claim 27 has structure implied by the step of transfecting a gene into the human cell strain; thus, having a gene inside the human cell. However, the genus of claimed human cell strains of claims 22-25 and 27-30 encompasses widely varying species of mutated human cell strains by mutating from human myeloma cells; mutated from RPMI226 or mutated from KMS-12M; wherein the mutation is unlimited (e.g., a gene deletion, substitution, addition or any combination thereof, for example); thus, the structural limitation implied by the term "mutated" is open to encompass any structure as long as the cell is human cell strain or human cell origin. To fully describe a genus of mutant recombinant nucleic acid molecules, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. The prior art by Kawahara et al. (1999, Human Antibodies, Volume 9, pages 83-87), Pene et

al. (Oncogene, 2002, Volume 21, pages 6587-6597, as cited previously) and Hata et al. (Clin Exp Immunol, 1994, Volume 94, pages 370-375) teach a species of mutated human cells encompassed by the claimed genus of human cell strains as noted below 35 U.S.C. 102. The specification discloses two species of claimed human cell strain (i.e., SC-02MFP having the Accession No. FERM BP-10078 and SC-01MFP having the Accession No. FERM BP-10077) which can be used for a production of protein as described in Claims 22 and 29. However, the prior art and the instant specification do not describe representative species of human cell sufficiently to reflect the variation among the members of the genus nor do the prior art and specification disclose a correlation between the structure of any human cell strain and function of continuous, long term, and stable production of any protein from an exogenous gene in Claims 22-25 and 27-28. The prior art and the instant specification do not describe representative species of human cell sufficiently to represent the correlation between the structure of any human cell strain and function of continuous production of any protein from an exogenous gene at a yield of 1 ng to 10 ug/day per 10^6 cells at least over a 2-month period as recited in Claims 29-30. Thus, the instant specification and the prior art cannot describe the structure of a very broad claimed genus and one skilled in the art would not be in possession of the claimed genus by the instant specification.

6. Claims 22-25 and 27-30 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for the human cell strain SC-02MFP having the Accession Number FERM BP-10078 or SC-01MFP having the

Accession Number FERM BP-10077; does not reasonably provide enablement for any human cell strain as broadly encompassed by the claims.

The specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use of the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The nature of the invention is drawn to human cell strains SC-02MFP having the

Accession Number FERM BP-10078 or SC-01MFP having the Accession Number FERM BP-10077.

The breadth of claim includes any human cell strain (including but not limited to any mutant strain of any human myeloma cell) which may be capable of producing a protein from any exogenous gene at a yield of 1 ng-10 ug/day per 1,000,000 cells for at least a 2-month period or at least over a 2 month period; because the protein production capability recited in claims can be interpreted as requirement for the cell before the mutation wherein the claimed human cell is the mutated version; wherein the step of mutation is not limited in anyway (e.g., a gene deletion, substitution, addition or any combination thereof, for example); thus, the structural limitation by the term "mutated" is open to encompass any structure as long as the cell is human cell strain or human cell origin.

The state of prior art, guidance and working example(s): The prior art by Kawahara et al. (1999, Human Antibodies, Volume 9, pages 83-87), Pene et al. (Oncogene, 2002, Volume 21, pages 6587-6597, as cited previously) and Hata et al. (Clin Exp Immunol, 1994, Volume 94, pages 370-375) teach a species of mutated human cells encompassed by the very widely varying genus of claimed human cell as noted below 35 U.S.C. 102. The specification discloses two species of claimed human cell strain (i.e., SC-02MFP having the Accession No. FERM BP-10078 and SC-01MFP having the Accession No. FERM BP-10077) which can be used for a production of protein as described in Claims 22 and 29. Applicants disclose no direction or guidance on how to make and use any other human cell strain that is any mutant of human

myeloma cell strain. Therefore, it is unpredictable for any human cell strain to be used in the continuous production of any desired protein as described in Claims 22 and 29. Thus, it is unpredictable for any human cell encompassed by the claims for one skilled in the art to make and use the full scope of claims. The said unpredictability makes the relative skill required in the art very high. For all of the above reason, it would require undue experimentation necessary for any human cell strain.

Withdrawn-Claim Rejections - 35 USC § 102

7. The previous rejection of Claim 20 under 35 U.S.C. 102(b) as being anticipated by Pene et al. (Oncogene, 2002, Volume 21, pages 6587-6597) is withdrawn by virtue of Applicants' declaration (filed 3/3/2009) disclosing the difference between the SC-02MFP and the KMS-12BM by Pene et al.

8. The previous rejection of Claim 21 under 35 U.S.C. 102(b) as being anticipated by Hata et al. (Clin Exp Immunol, 1994, Volume 94, pages 370-375) is withdrawn by virtue of Applicants' declaration (filed 3/3/2009) disclosing the difference between the SC-01MFP and the PRMI8226 by Hata et al.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Pene et al. (Oncogene, 2002, Volume 21, pages 6587-6597, as cited previously).

Claim 22 (Claims 23-25 dependent therefrom) is drawn to a human cell line strain which is from human myeloma cell strain established by method recited in the claim. Claims 23-25 are drawn to the human cell strain with additional method steps.

Claim 22 encompasses any human cell strain having a product by process type limitation, which "ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS" (see MPEP 2113 [R-1]). In the instant case, only structure implied by the steps is that the claimed human cell strain has to be originated from a human myeloma cell; whereas the obtaining and selecting step (although it describes the physical characteristics) does not contribute or imply any structure of the claimed human cell strain for the following reasons. Because the step b) and d) of selecting mutated clones having "a doubling time of 18 to 24 hours and a 90% rate of cloning" is identical, the selected mutant clones do not contribute or imply any structure of claimed human cell strain. In regards to "wherein the clones selected are capable of producing .... for at least a 2-month period" (emphasis added), this only further describes "the clones" which is before the inducing mutation wherein the claimed human cell is a mutated version (or at least claimed to be mutated because one can assume that any selected cell is mutated since it is to be selected after the induction step). Thus, the claimed human cell strain (i.e., mutated clones by virtue of all

four steps a to d) is not necessarily required to have the recited limitations of "wherein the clone...". Also, the clones selected only need to be capable of producing a protein as recited in Claim 22; wherein the recitation of "capable of" is broadly but reasonably interpreted as encompassing a *potential* property of the clones, which, as evidenced by the instant specification and applicant's instant remarks at p. 6, top, is a *potential* property of a RPMI8226 cell of Pene. Thus, the clones are not necessarily required to actively produce protein as described at the end of Claim 22. Claims 23-24 only further describe the method steps which do not contribute or imply any structural limitation of claimed human cell strain.

For the reasons above, Pene et al. teach the human myeloma cell "RPMI8226" (the cell used to make instant SC-02MFP) which is encompassed by the **Claims 22 and 25**. Claims 23-24 only further describes the method steps which do not contribute or imply any structural limitation of claimed human myeloma cell; and the claims does not require any structural limitation(s) to be met from the cell of claim 22; thus, the human myeloma cell "RPMI8226" meets the limitation of **Claim 23-24**.

10. Claims 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Hata et al. (Clin Exp Immunol, 1994, Volume 94, pages 370-375).

Claim 22 (Claims 23-25 dependent therefrom) is drawn to a human cell line strain which is from human myeloma cell strain established by method recited in the claim. Claims 23-25 are drawn to the human cell strain with additional method steps.

Claims 22-25 have been broadly, but reasonably interpreted as noted above. Similarly, the clones selected only need to be capable of producing a protein as recited in Claim 22; wherein the recitation of "capable of" is broadly but reasonably interpreted as encompassing a *potential* property of the clones, which, as evidenced by the instant specification and applicant's instant remarks at p. 6, top, is a *potential* property of a KMS-12BM cell of Hata.

For the reasons above, Hata et al. teach the human myeloma cell "KMS-12BM" (which is used to make instant SC-01MFP) which is encompassed by the **Claims 22 and 25**. Claims 23-24 only further describes the method steps which do not contribute or imply any structural limitation of claimed human myeloma cell; and the claims does not require any structural limitation(s) to be met from the cell of claim 22; thus, the human myeloma cell "KMS-12BM" meets the limitation of **Claim 23-24**.

11. Claims 22-24, 27 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Karpas et al. (PNAS, 2001, Volume 96, pages 1799-1804). Instant rejection is necessitated by Applicants' amendment.

Claim 22 (Claims 23-24 and 28 dependent therefrom) is drawn to a human cell line strain which is from human myeloma cell strain established by method recited in the claim. Claims 23-24 are drawn to the human cell strain with additional method steps. Claim 27 are drawn to the human myeloma cell further comprising transfecting a gene encoding a desired protein into the human cell strain.

Claims 22-25 have been broadly, but reasonably interpreted as noted above. It is noted that Claim 27 recites "further comprising transfecting a gene encoding a desired protein into the human cell strain"; thus, imply that it must have a gene encoding a desired protein in the human cell strain.

Karpas et al. teach "A human myeloma cell line suitable for the generation of human monoclonal antibodies" as shown in title; wherein the human myeloma cell line is used to form a hybridoma by fusing "164 cells" (i.e., IgG producing EBV-immortalized B cells; thus, contain a gene encoding the IgG); wherein the hybridoma cell meets the limitation of any human cell strain from a human myeloma cell strain as in Claims 22-24. The transfection step is not limited in anyway and it can be interpreted broadly and reasonably as "incorporation of exogenous DNA into a cell" (see transfection in the attachment). Thus, the exogenous IgG gene encoding the IgG polypeptide has been incorporated into the hybridoma cell by Karpas et al. and thus, meets the limitation of broad and reasonable interpretation of "transfecting a gene" in Claim 27 and having a gene encoding a desired protein in the human cell strain.

Although, Claim 29 recites "capable of ...", this limitation does not require the human cell strain to actively produce the protein at the yield as recited in Claim 29 as long as the human cell strain has *potential* to do so. Karpas et al. teach "Most of the 40 hybridomas maintained continuously in culture have been secreting Ig during the past 5 months" (see bottom of page 1800, left column). Karpas et al. teach an Ig secretion condition in the description of Fig. 1 on page 1800, which disclose the cell were "incubated for 8 h at 37^{o}C in a CO_2 incubator (see line 5 of the description). Karpas et

al. also teach "human hybridomas can produce 210 ug of IgG per ml...$9x10^5$ cells per milliliter, that is, approximately 0.0035 ug per hybridoma cell" (i.e., 2.5 ng/cell) after transfection with human Ig genes. see bottom left column to top right column, page 1804), which satisfies the yield limitation of Claim 29. Thus, the hybridoma cell of Karpas et al. is capable of (emphasis added) producing much less protein (Ig) at a yield of 1 ng to 10 ug/day per 10^6 cells at least over a 2-month period continuously with an appropriate condition; thus, meeting the limitation of Claim 29.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. Claims 22-24 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Karpas et al. (PNAS, 2001, Volume 96, pages 1799-1804) in view of Kawahara et al. (1999, Human Antibodies, Volume 9, pages 83-87, as cited previously) and Toneguzzo et al. (Molecular and Cellular Biology, 1986, Vol. 6, pages 703-706).

In view of the teachings noted above by Karpas et al., the human-human hybridoma of Karpas et al. meets the limitation of Claims 22-24 and 27 and 29.

Karpas et al. further disclose that "over the past 20 years we have developed several human myeloma cell lines from six different patients with myeloma, and one of

them has been adapted to be used as a partner for the derivation of human-human hybridomas" (see end of introduction on page 1799, left column) and the monoclonal antibodies produced may have advantages in immunotherapy (see end of the abstract).

Karpas et al. does not teach culturing the disclosed human cell strain in a serum free medium (Claim 28).

Kawahara et al. teach a new human fusion partner, ICLU-T for a making hybridomas; wherein ICLU-T was prepared from human T cell acute lymphocitic leukemia PEER (see left column on page 83 and see "Preparation of a human parent cell line from t-lymphoma" in the middle of left column on page 84); wherein the hybridomas grows in serum free medium.

Toneguzzo et al. teach electric field-mediated DNA transfer for stable gene expression in human lymphoid cells.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to make a human hybridoma cell of Karpas et al. with the fusion partner ICLU-T of Kawahara et al. with a reasonable expectation of success because making a human hybridoma using two fusion partner taught by Karpas et al. and Kawahara et al. for the purpose of expressing a protein of interest such as monoclonal antibodies, for example; and furthermore, the transfection of any gene encoding a protein of interest into a human lymphoid cell (the cell of Kawahara et al., for example) is taught by Toneguzzo et al. (1986) for enabling the human cell as a host to express a protein of interest. The motivation to use ICLU-T of Kawahara et al. as a hybridoma fusion partner for culturing expressing and producing a protein of

interest by culturing the hybridoma in a serum free medium is provided by Kawahara et al. who teaches that "to purify the many kinds of products from T cells, it was stated that serum free culture was more useful than serum culture because of no effects of unknown components contained serum" (see right column lines 6-8, page 83) which is important for any protein that would be used for therapeutic use (such as monoclonal antibodies as disclosed by Karpas et al.); and the hybridoma do not lose the ability to produce a protein (e.g., encoded by the transferred gene encoding immunoglobulin IgG) over many months of continuous growth as shown by Karpas et al. which is advantageous for any protein production (see end of abstract). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 10AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/
Examiner, Art Unit 1656

/David J. Steadman/
Primary Examiner, Art Unit 1656